**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 39862

**Title:** Role of colectomy in preventing recurrent PSC in liver transplant recipients

Dear Prof Ma,

Thank you very much for your interest in our manuscript. The helpful comments of both the Editor's and the Reviewers are much appreciated and the manuscript has been appropriately revised. We have addressed all the comments both in the revised manuscript and in the point-to-point response below. The revised manuscript has been re-formatted as requested by the Editor. We have also checked the reference list and confirm that the list does not contain any duplicates of references.

We hope this revised version is to the satisfaction of the Editorial board and the Reviewer's and would like to thank them for their academic input which helped to improve the quality of this manuscript.

**Reviewer Comments**

**Reviewer # 02530754**

The present manuscript by Buchholz BM et al. is a nice systematic review which aimed to evaluate the role of profilactic colectomy in liver transplant patients with PSC in order to prevent post-LT disease recurrence. The authors concluded that pre/peri transplant colectomy may have a protective role in this scenario but no randomized trials are available and therefore no strong recommendation can be made. The manuscript is informative and reads well. The literature search strategy is updated. The topic is attractive and timely.

The authors are kindly invited to consider the following minor comments:

1. The authors said that "literature search was independently conducted by 2 authors (B.M.B, P.M.L.)". If any disagreement was found, I presume that a third author resolved it. If it is so, please add a statement in methods.

Thank you very much for pointing this out. We have now explicitly stated in the methods that, similar to our approach of discrepancies in the quality assessment of the selected studies by MINORS criteria, any disagreement in the literature search was resolved by a third author (G.K.F.)

2. The literature search strategy is not sufficiently clear and 180 initial records seemed to me too few. I would recommend including a supplementary table including the combinations of MESH terms used.

We greatly appreciate this important comment and are pleased to follow the reviewer's recommendation to add a supplementary figure outlining the literature search strategy including the combinations of MESH terms used for clarification. The figure has been labeled as Supplementary Figure S1. The accuracy of the number of the initial records retrieved by our literature search in ensured as it was independently conducted by 2 authors and we have repeated the search yielding similar results.

3. Although the quality of the studies included according to the MINORS criteria was overall reported as high, the authors admitted that all of them were observational, retrospective and some of them insufficiently powered. There is an inherent increased risk of bias given that patients undergoing colectomy are clinically selected, and probably had a more severe IBD. Therefore it is highly probable that the protective role of colectomy may have been underestimated in the available studies. In my opinion, this aspect should be further discussed. Conclusions may be also softened while

emphasizing the need of prospective studies and randomized trials.

We are in agreement that severe colonic inflammation is a leading indication for colectomy in both the pre- and post-transplant setting as stated in the discussion. Whether the clinical selection of patients undergoing colectomy has led to an underestimation of the protective role of colectomy is difficult to answer. We have therefore opted not to add this point to the discussion but rather believe that investigating IBD presence and time of IBD diagnosis as secondary outcome has sufficiently covered this aspect while being based on available data. Regarding the second aspect of this reviewer's comment, we have reworded the section in our conclusions (page 19) and have elaborated on the limitations of the research conclusions in the article highlights. We have also stressed the need for prospective studies and randomized trials in both the article highlights and the core tip.

4. I agree with the authors that a universal colectomy in PSC transplant candidates may not be currently justified in light of the available evidence. However, there are subgroups of patients with high risk of an aggressive recurrence such as young patients with early graft loss (<5 years) because of recurrent PSC in whom a retransplantation is being considered. In opinion of the authors, is profilactic colectomy advisable in this clinical context? I know there is little supporting evidence but some speculation here would be welcomed.

We take the reviewer's point and equally find this interesting. We believe that retransplantation for rPSC is accepted practice, certainly in the UK as published in the literature. An interesting aspect to consider is in which patient groups would a prophylactic colectomy actually be beneficial in order to decrease the risk of developing rPSC; which has been demonstrated to be associated with an increased risk of graft loss. The value of colectomy in LT candidates for regrafting caused by rPSC has not been investigated in the included studies, and therefore this approach remains speculative.

**Reviewer # 03253490**

Buchholz et al. reviewed 'The published evidence on the role of colectomy in preventing rPSC in LT recipients.' The focus of the review is very interesting. The review is well written and has enough priority for publication.

We are delighted to receive such positive feedback on out work.